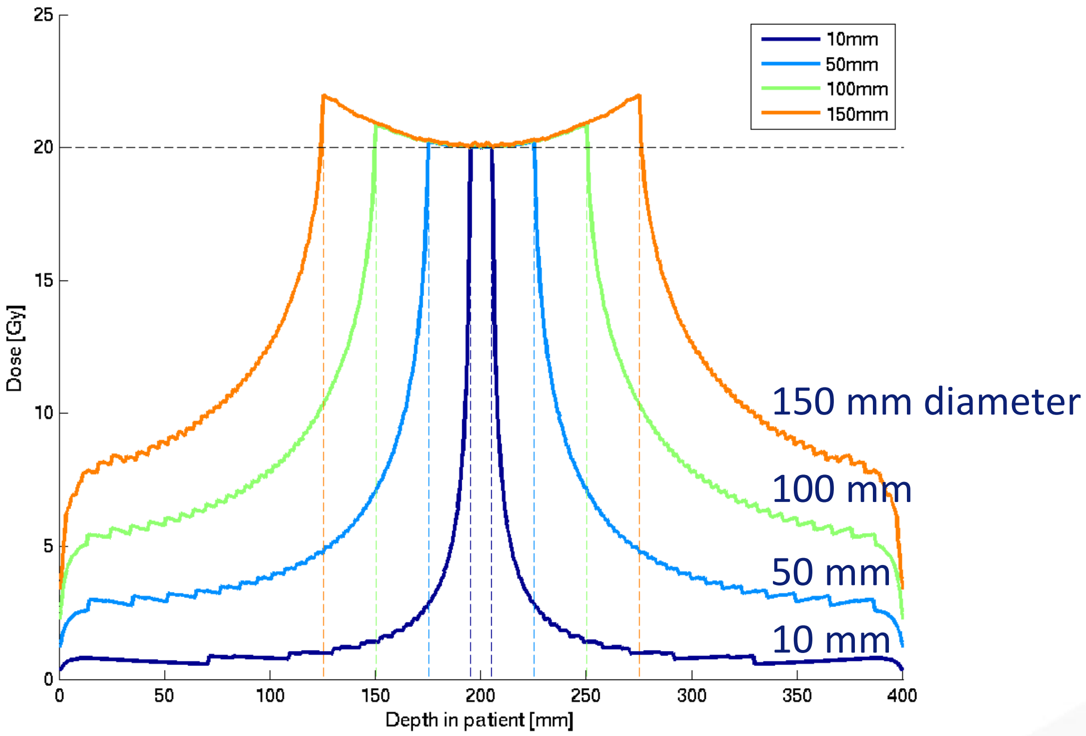
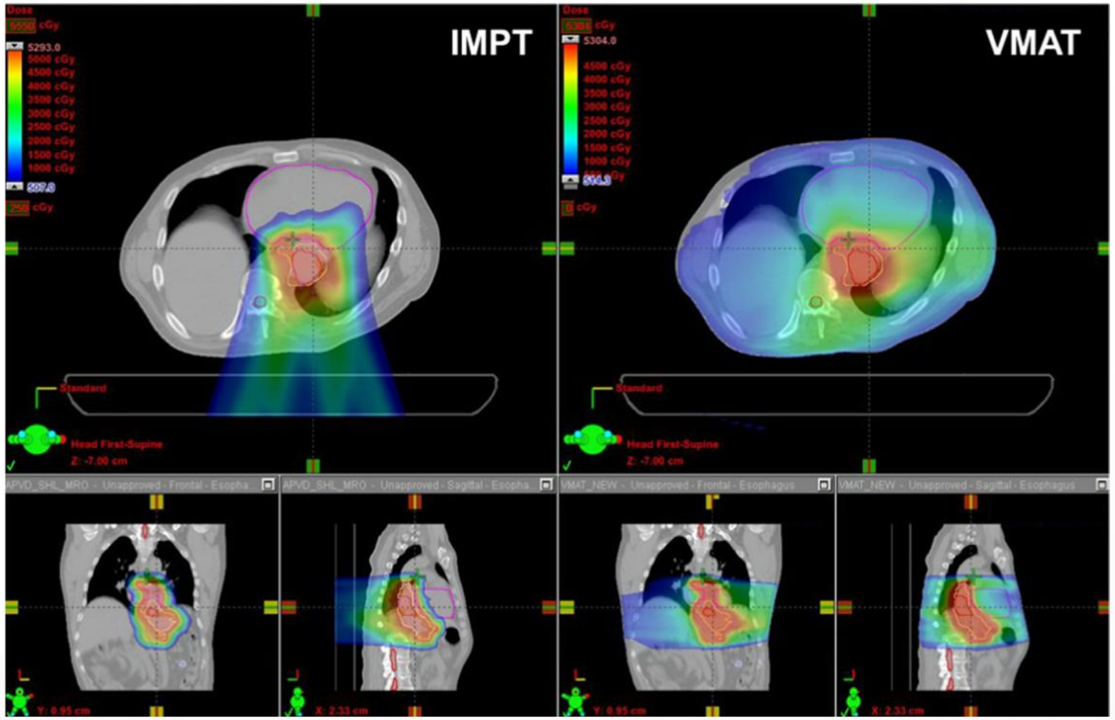
De uitdagingen en kansen bij protonentherapie voor longkanker

RT Themadag Eindhoven

Protons Yield Better Dose Distributions





Liao et al. Semin Radiat Oncol 28:114-124

It’s All About Physics Where the Protons Stop

electron density

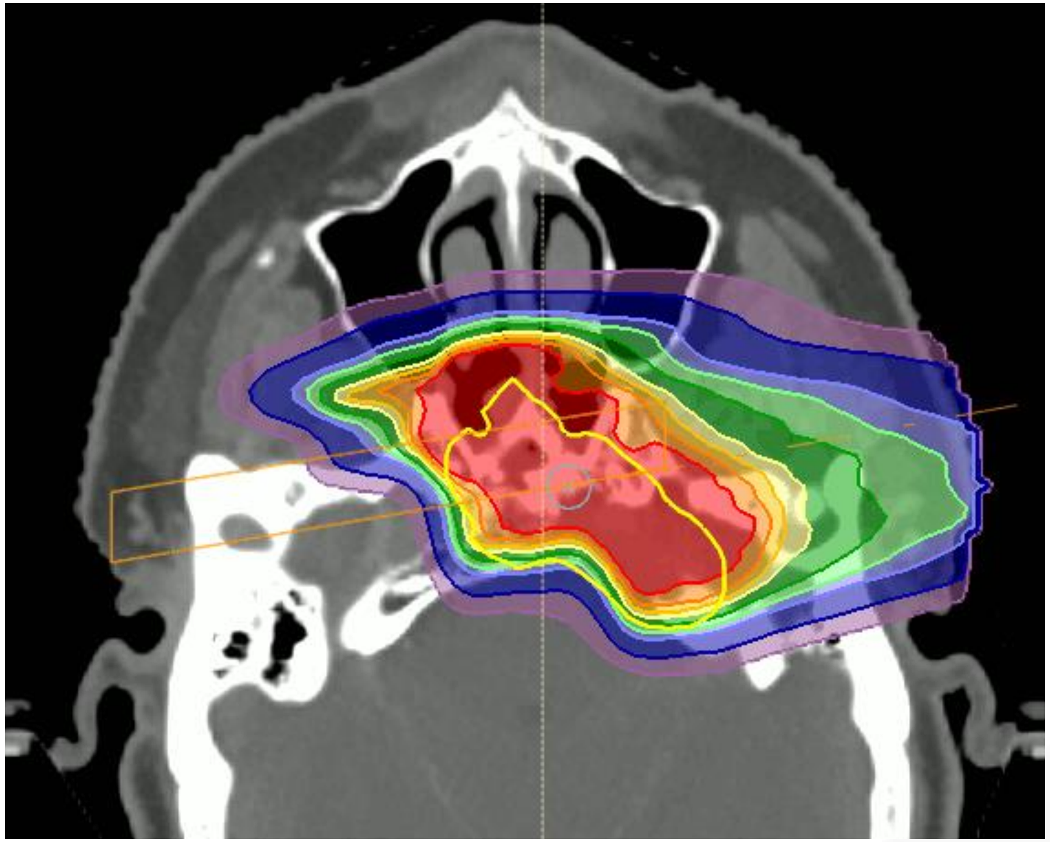
$$S = -\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{nz^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0}\right)^2 \cdot \left[ln\left(\frac{2mec^2\beta}{I \cdot (1-\beta^2)}\right) - \beta^2\right]$$

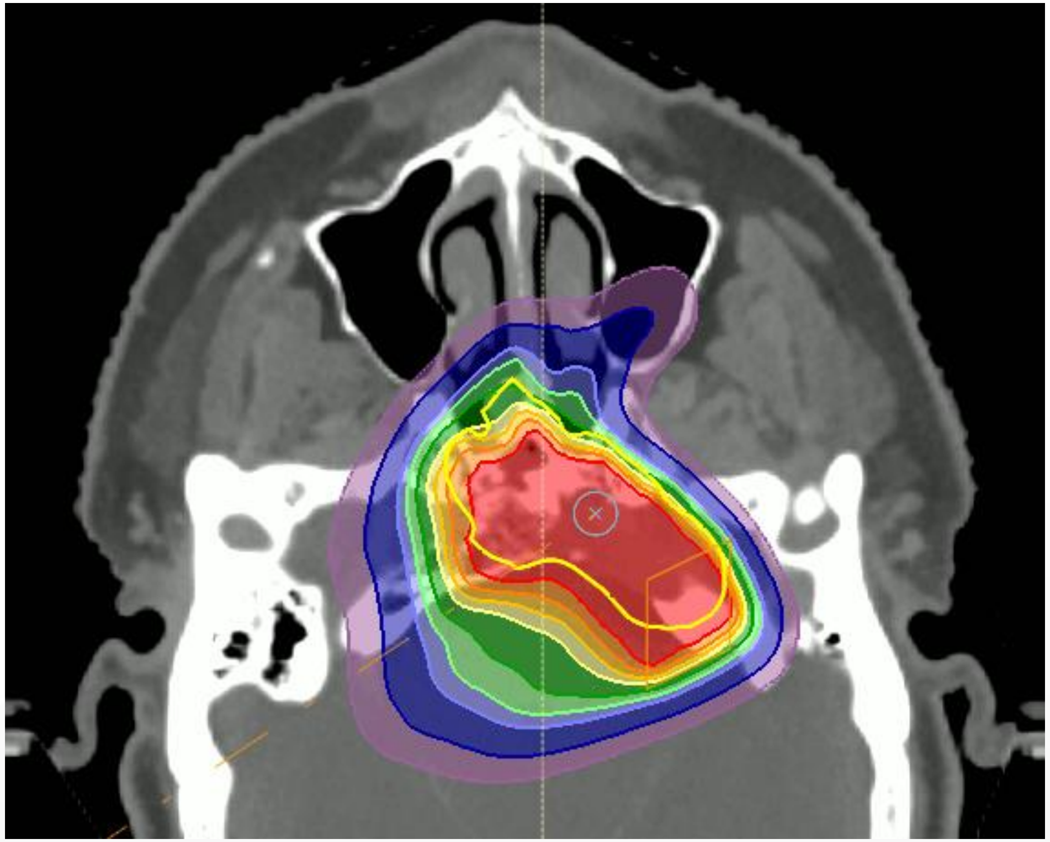
v/c of protons

mean excitation potential

energy loss

Dose Uncertainty

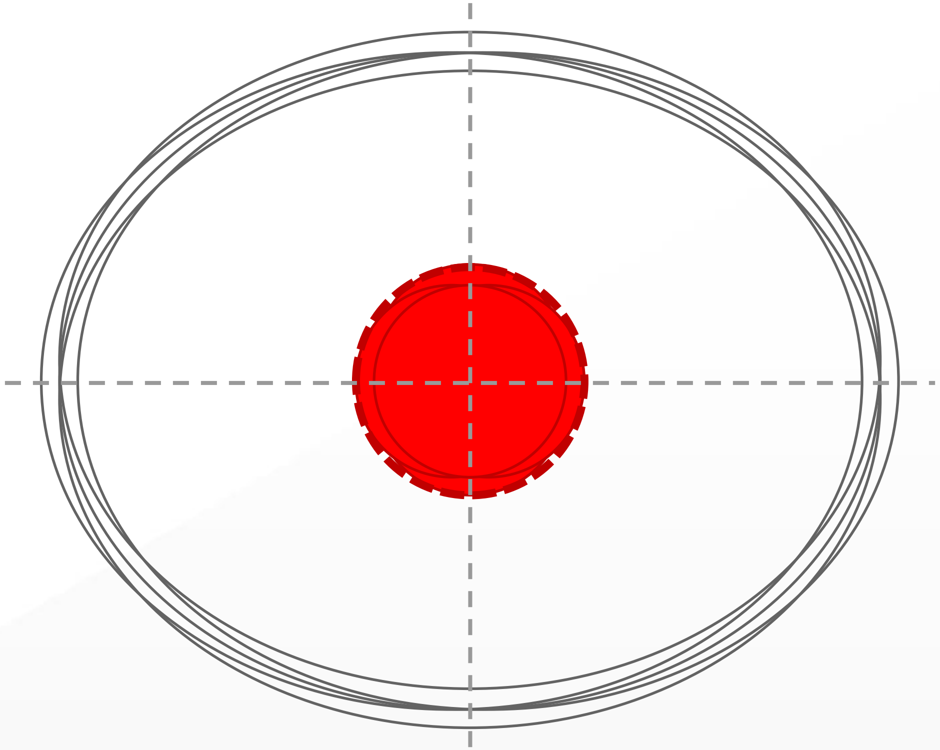




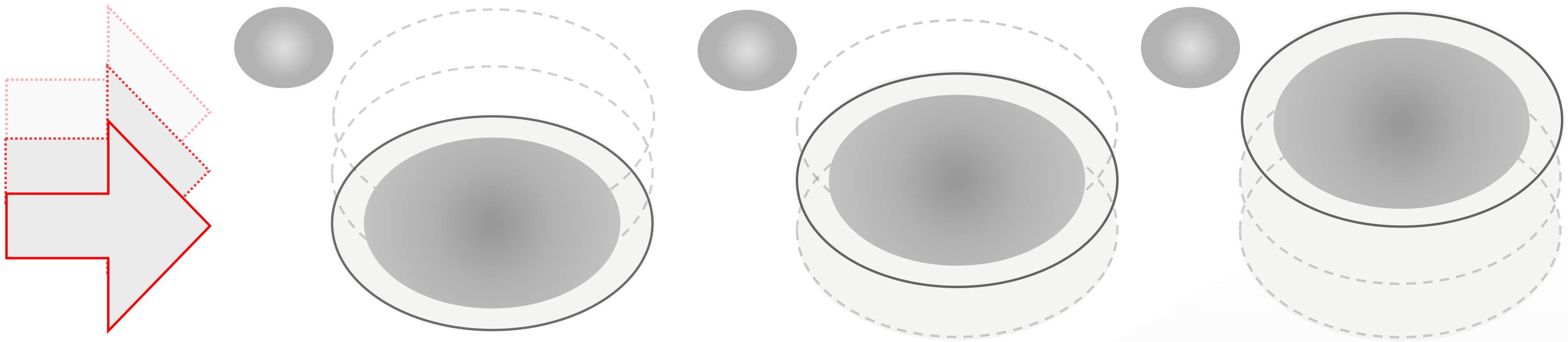
Robust Treatment Planning

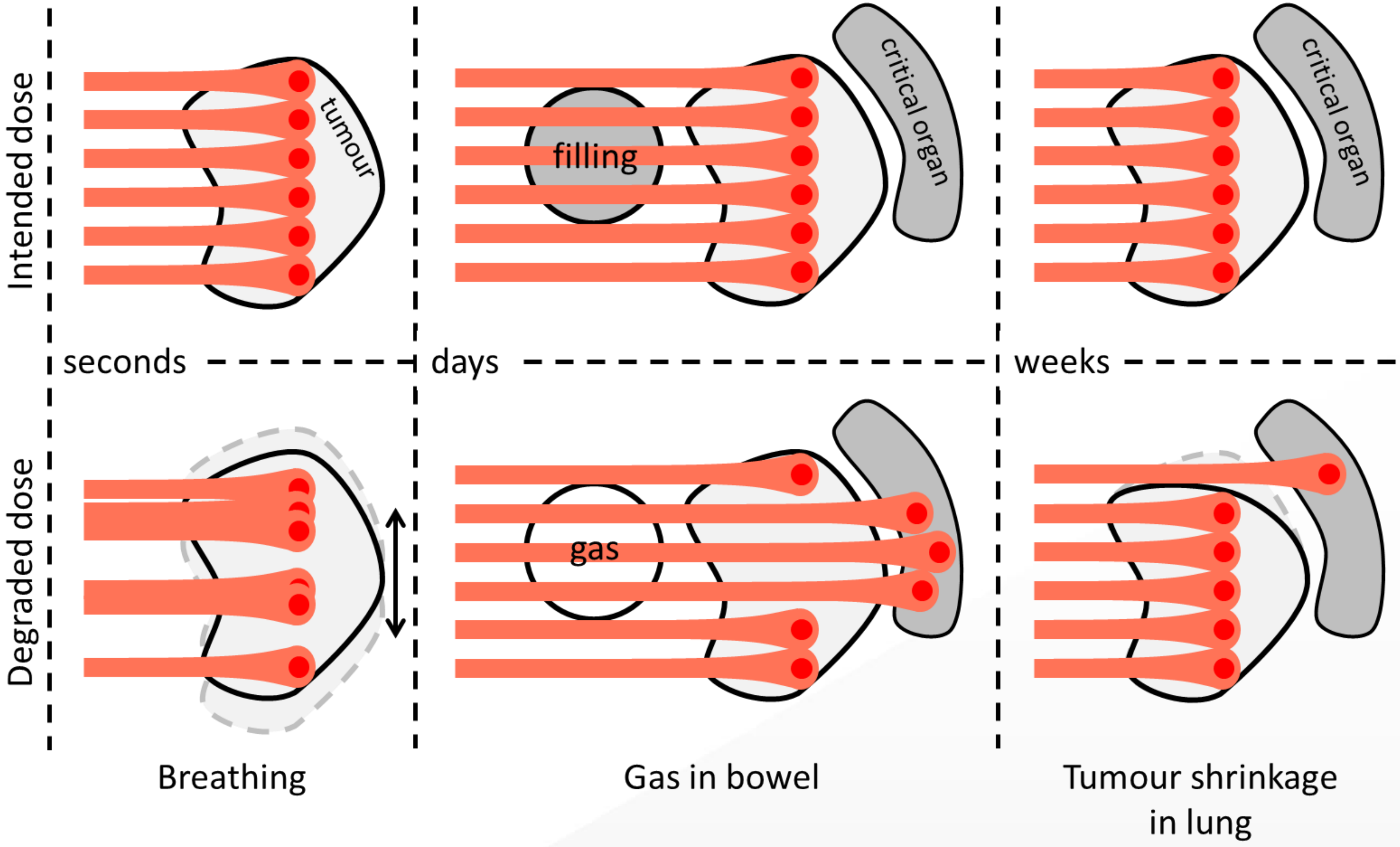
Accounts for density variations along the pencil beam paths

Include overshoots and undershoots of the pencil beams caused by stopping power uncertainties

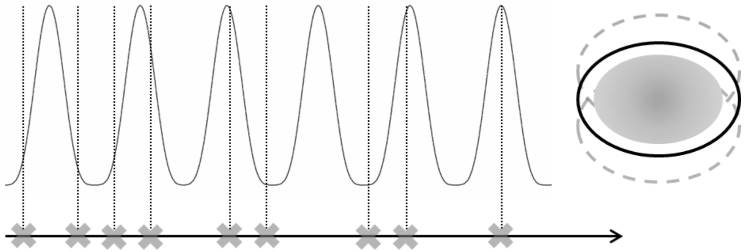


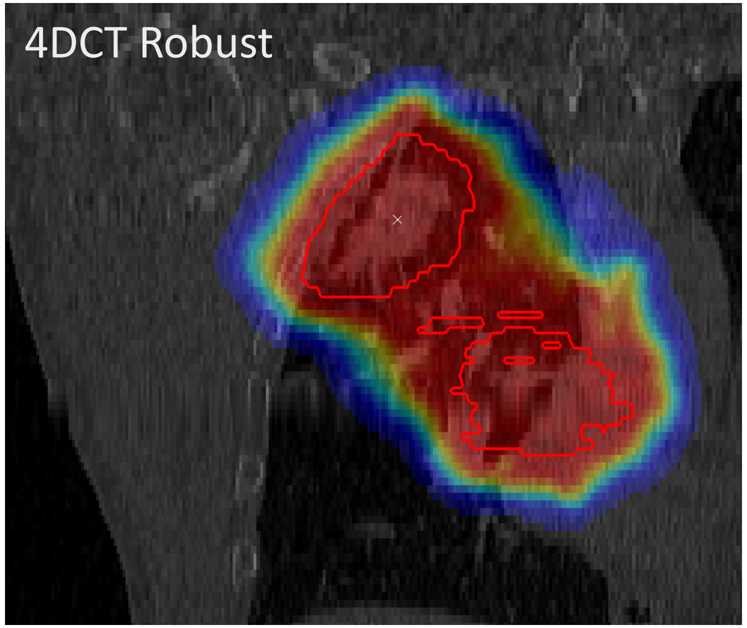
4DCT Robust Optimization

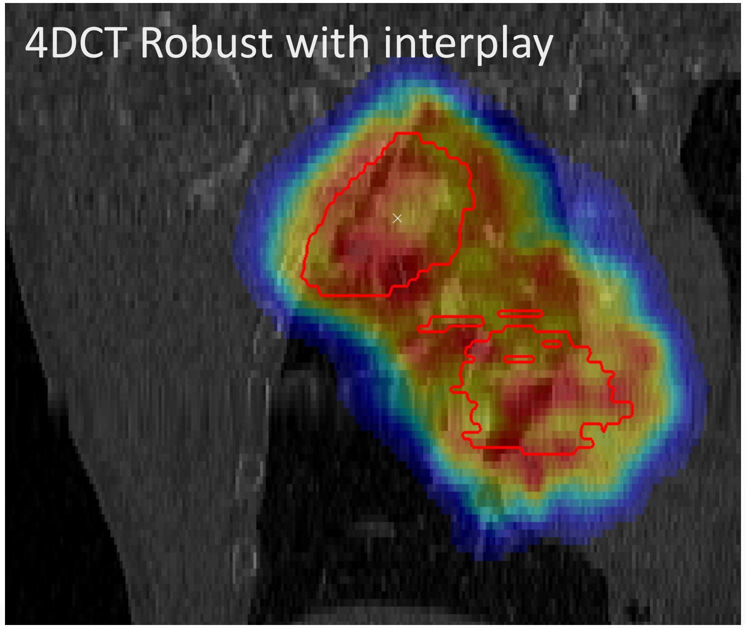


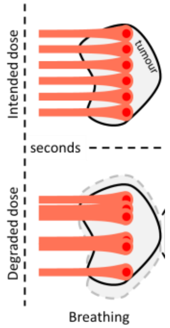

Intended dose
tumour
filling
critical organ
critical organ
seconds
days
weeks
Degraded dose
gas
Breathing
Gas in bowel
Tumour shrinkage
in lung

4DCT Robust Plans

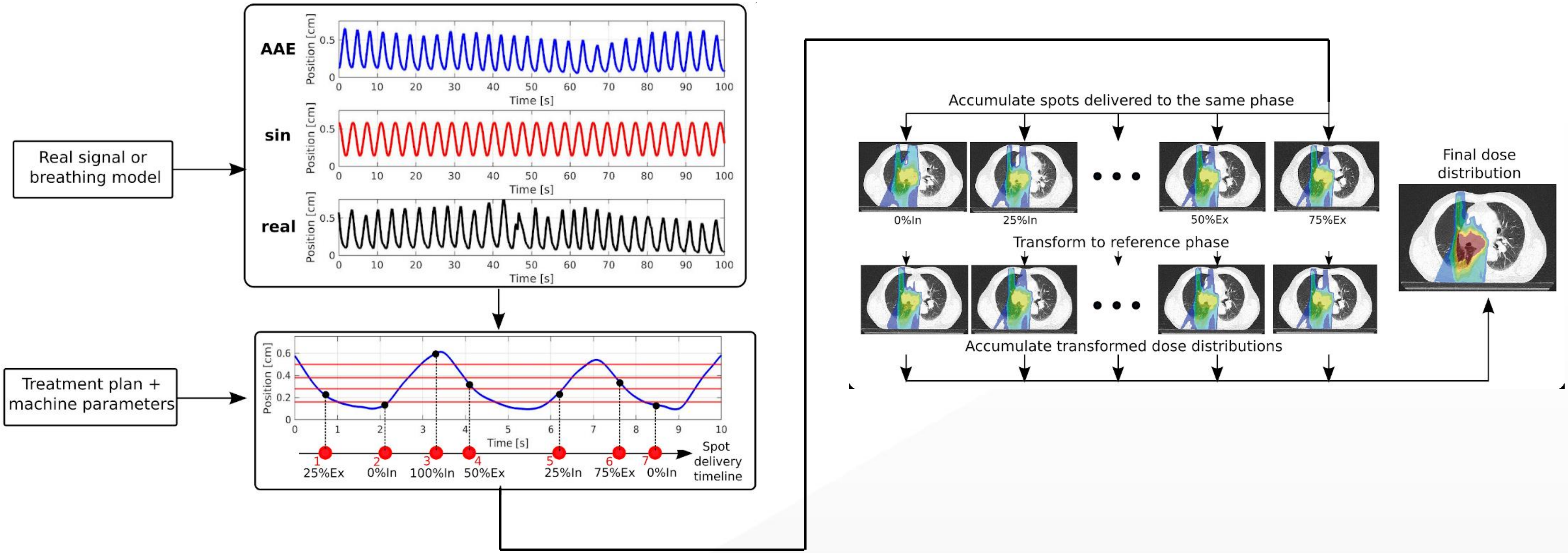




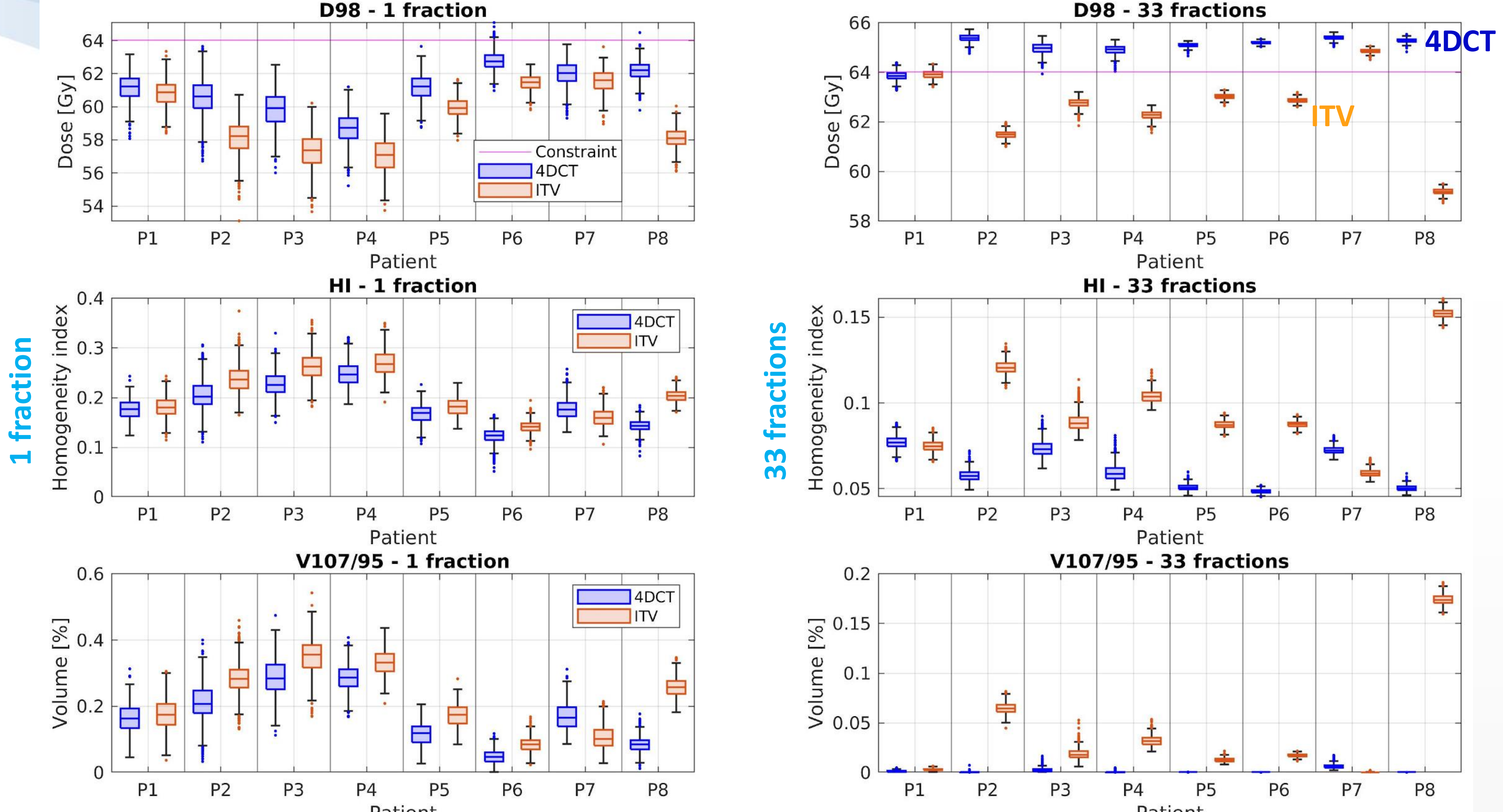




Oscar Pastor Serrano



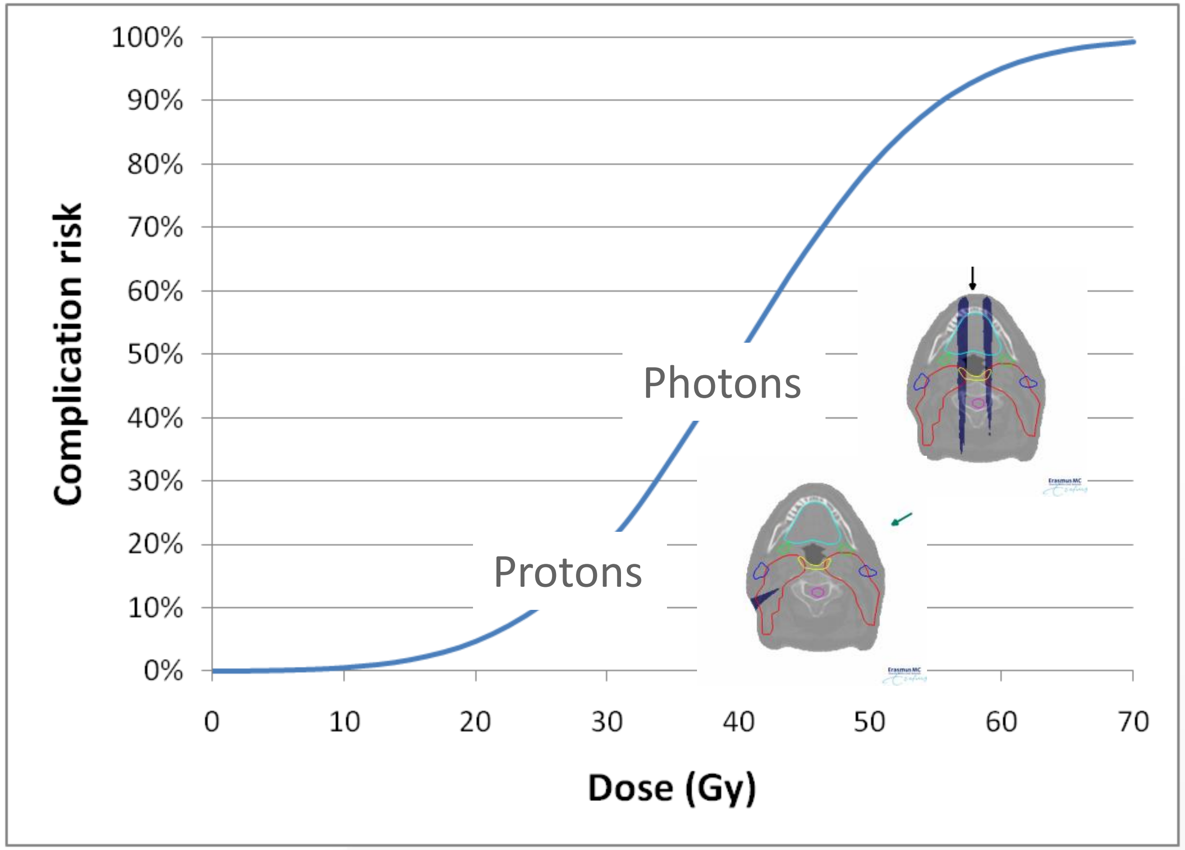
O. Pastor Serrano et al. accepted PMB (2021) and Pastor-Serrano, O., Lathouwers, D., & Perkó, Z. (2021). A semi-supervised autoencoder framework for joint generation and classification of breathing. Computer Methods and Programs in Biomedicine, 209, 106312



O. Pastor Serrano et al. Accepted in PMB (2021)

Toward clinical reality

ΔNTCP Based Patient Selection



National Indication Protocol

100% selected on risk of cardiac mortality

50% also on acute dysphagia and/or pneumonitis

Variabelen	NTCP-modellen		
	Radiatiepneumonitis* ≥ Graad 2 ≤ 6 maanden*	**Acute Dysfagie* ≥ Graad 2 ≤ 3 maanden***	**Mortaliteit (= graad 5) 2 jaar**
Discriminatie (c-statistic)	0.63	0.73 (0.70-0.76)†	0.64 (0.61-0.68)†
Kallibratie:			
Hosmer-Lemeshow test	0.46	0.171	0.023
Intercept	-0.24	0.003	-0.001
Slope	0.60	1.208	1.040
TRIPOD-type	Type 4	Type 4	Type 4
Evidentie niveau	Niveau 1a	Niveau 1b	Niveau 1b
ΔNTCP-drempel	≥10%	≥10%	≥2%

HollandPTC: Treatment Planning

Three beams with shortest distance to target volume

Planning on ITV with density override

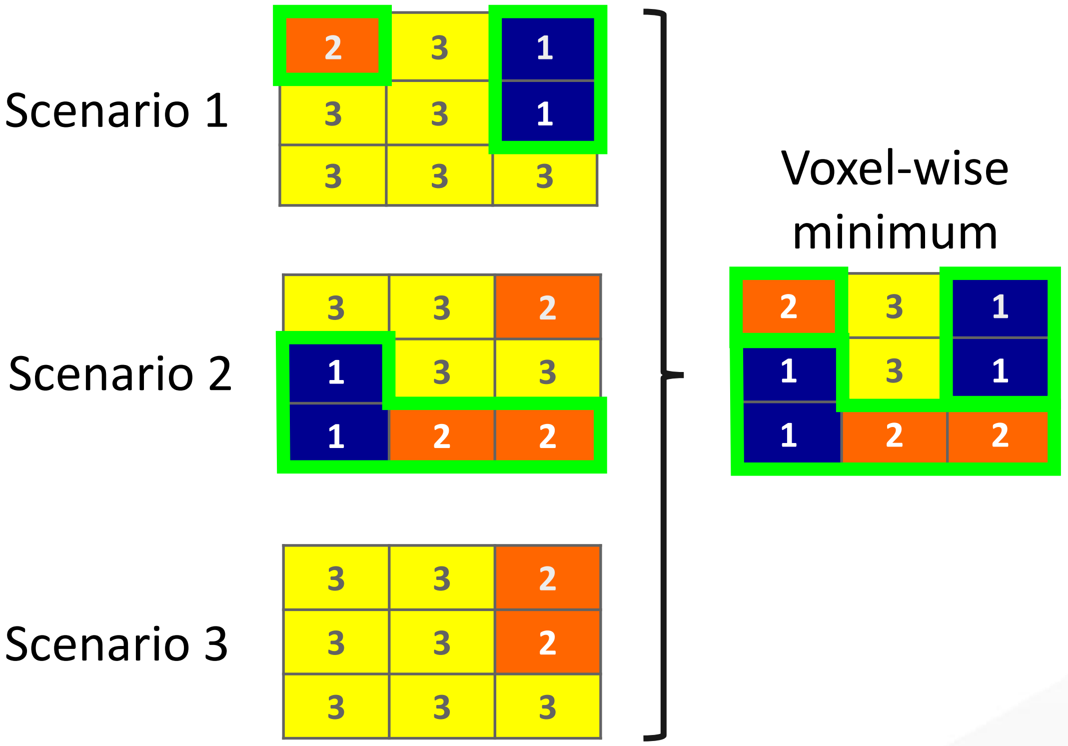
Robust optimization for setup and range errors (5 mm setup robustness; 2 mm ITV expansion; 3% range robustness)

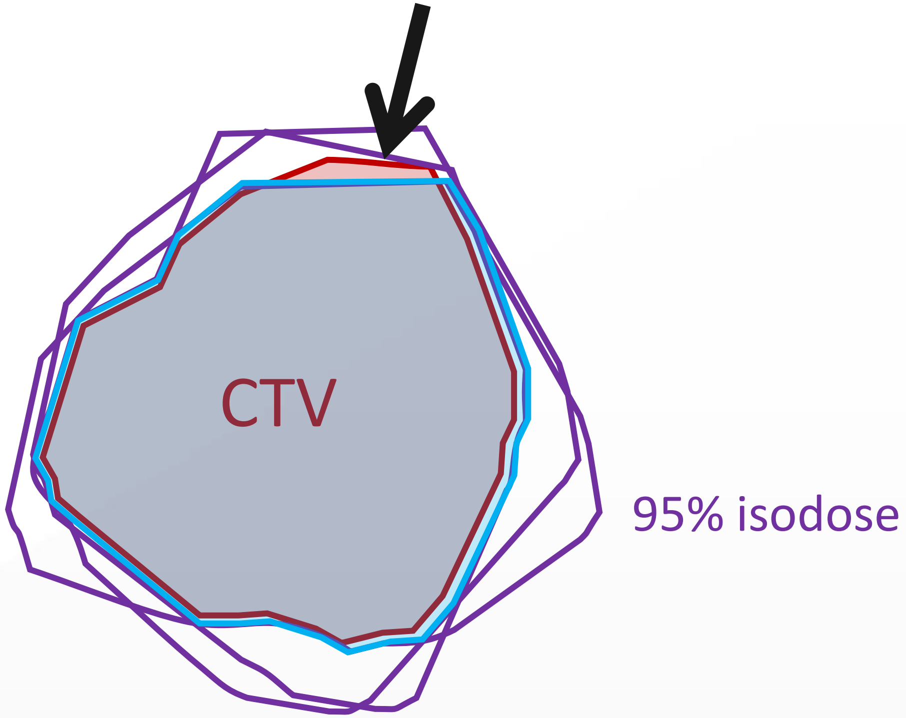
Optional larger spots

Optional 4D CT optimization on maximum inhale and exhale

95 %
90 %
80 %
70 %
60 %
50 %
40 %
30 %
20 %
8.3 %
Heart
CTV1
Esophagus
cord
Pos: (-143.9, -136.0, -1411.0) mm
Pos: (108, 286, 35) pixels
Slice: 36 of 107
Value: -90
Dose: 0.0 Gy
WL: -600
WW: 1600

Voxel-Wise Minimum Evaluation (Erosion)





Korevaar EW, Habraken SJM, Scandurra D, Kierkels RGJ, Unipan M, Eenink MGC, Steenbakkers RJHM, Peeters SG, Zindler JD, Hoogeman M, Langendijk JA. Practical robustness evaluation in radiotherapy - A photon and proton-proof alternative to PTV-based plan evaluation. Radiother Oncol. 2019 Dec;141:267-274.

HollandPTC Proton Therapy Centre | TU Delft | Erasmus MC | LUMC Leiden University Medical Center

DUPROTON Consensus Protocol

Number of scenario’s has been harmonized

Each institute determines the magnitude of the robustness setting depending on the accuracy of the treatment

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Practical robustness evaluation in radiotherapy – A photon and proton-proof alternative to PTV-based plan evaluation

Erik W. Korevaar [a,*], Steven J.M. Habraken [b,c], Daniel Scandurra [a], Roel G.J. Kierkels [a], Mirko Unipan [d], Martijn G.C. Eenink [b], Roel J.H.M. Steenbakkers [a], Stephanie G. Peeters [d], Jaap D. Zindler [b,c], Mischa Hoogeman [b,c], Johannes A. Langendijk [a]

[a] Department of Radiation Oncology, University Medical Center Groningen, University of Groningen; [b] Holland Proton Therapy Center, Delft; [c] Department of Radiation Oncology, Erasmus Medical Center Cancer Institute, Rotterdam; and [d] Proton Therapy Centre South-East Netherlands (ZON-PTC), Maastricht, The Netherlands

Evaluation

DUPROTON Consensus Protocol

Evaluation on 28 scenario's on CTV in mid position

Setup robustness 7 mm

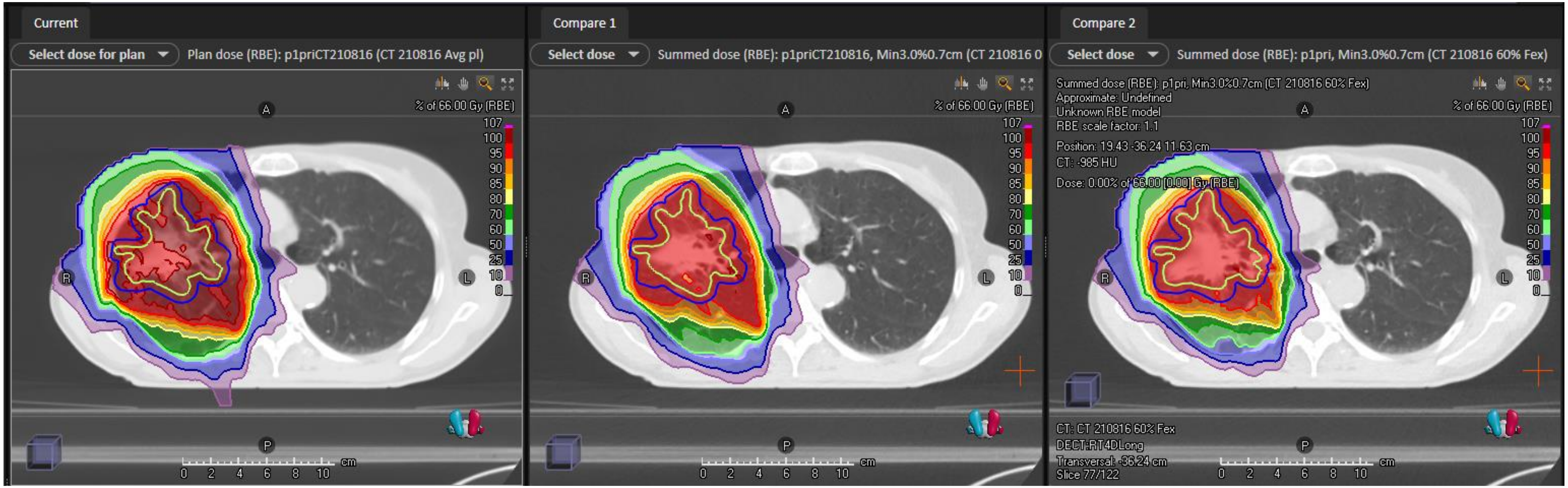
Range robustness 3%

Extra

In + ex phase of 4D CT

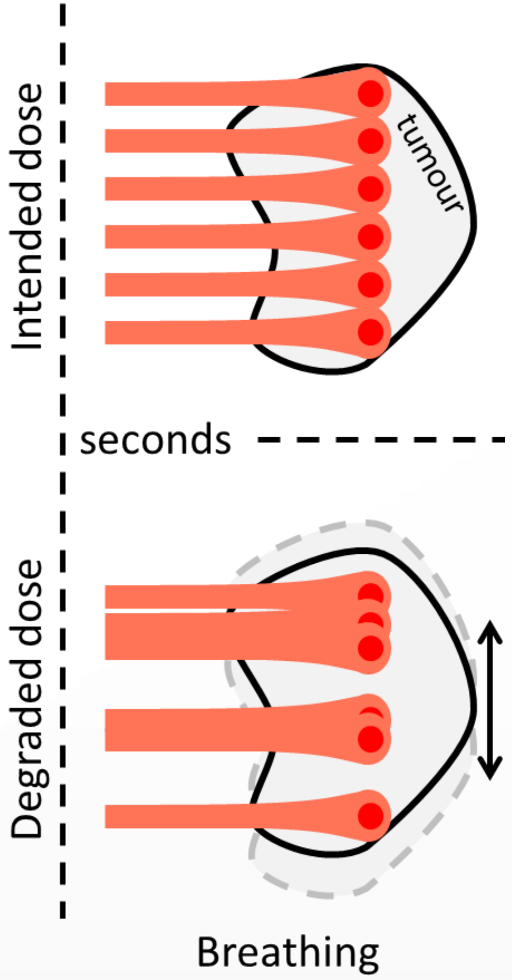
Evaluation

Nominal | Inhale-voxelwise min | Exhale-voxelwise min



Delivery

Use re-painting spots (amplitude >5mm)

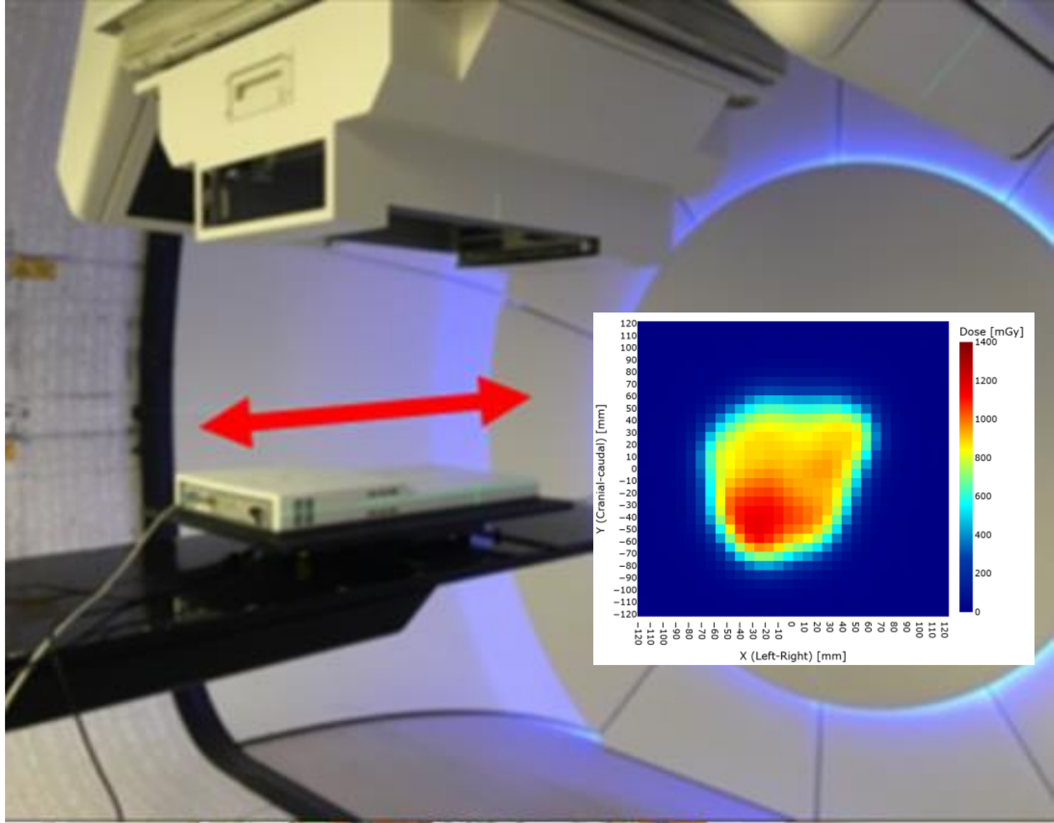


Repainting QA, how does it work?

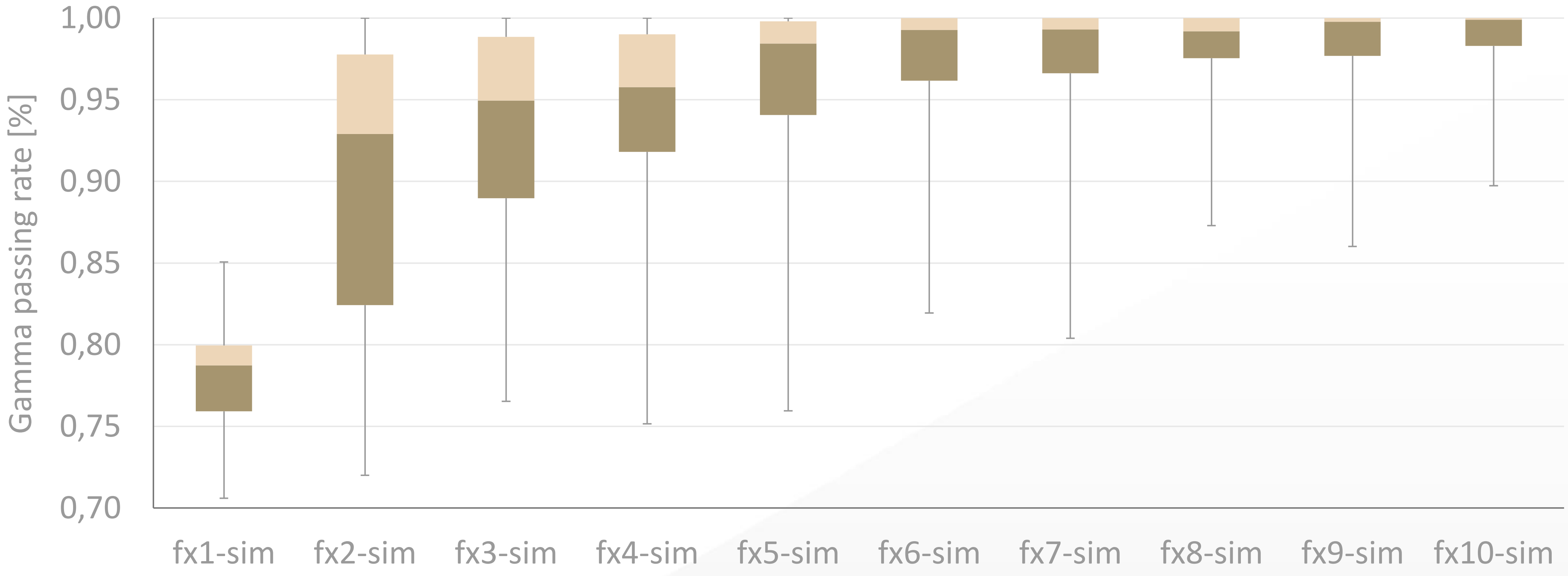
RayStation divides the spots and distributes them in time => repainting

We have verified that this yields the same dose distribution as without repainting

Hybrid test system to measure & simulate the impact of interplay on the dose distribution via patient-specific QA

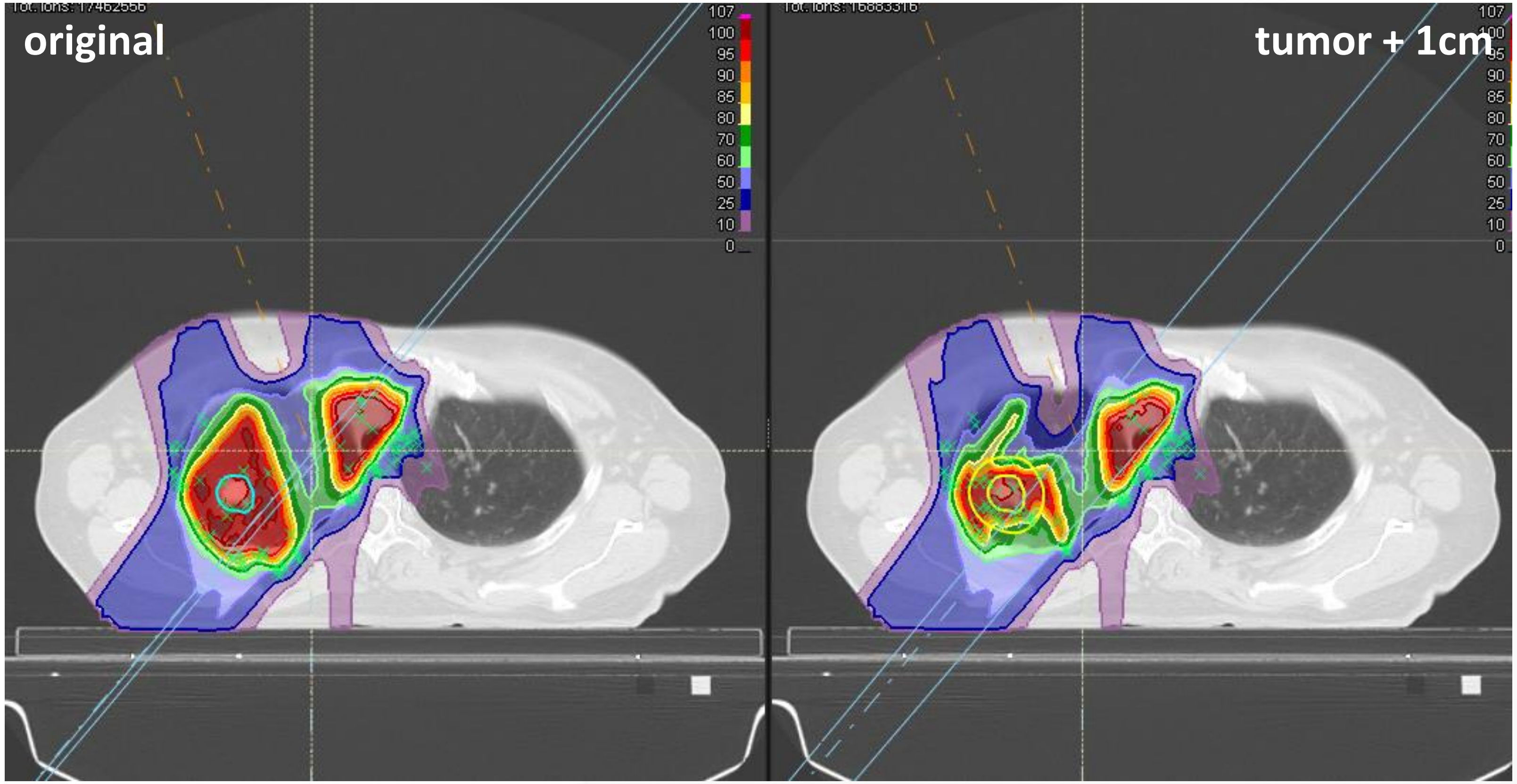


QA of Repainting

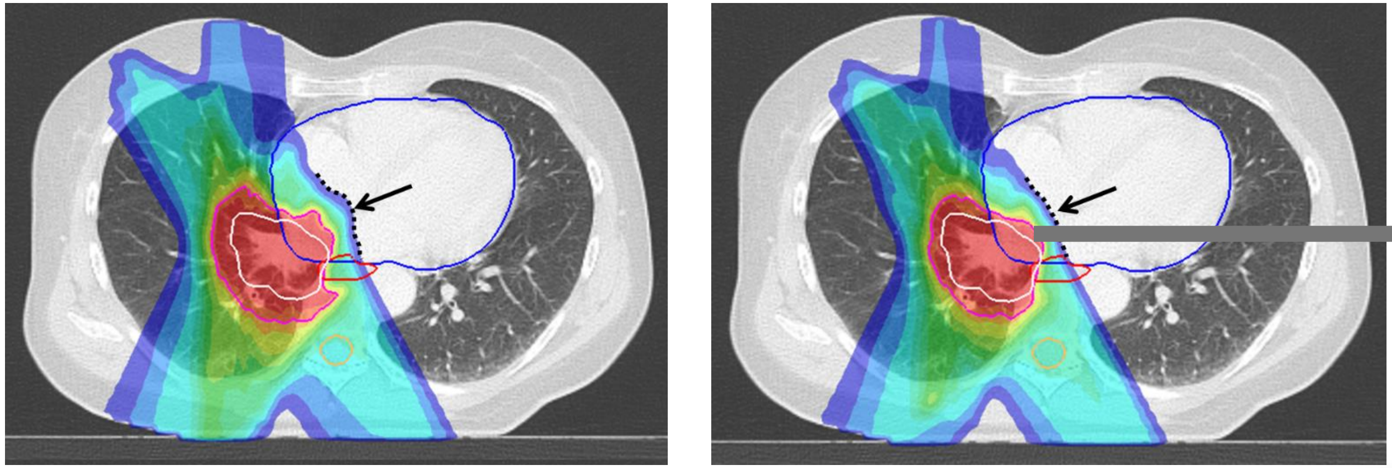


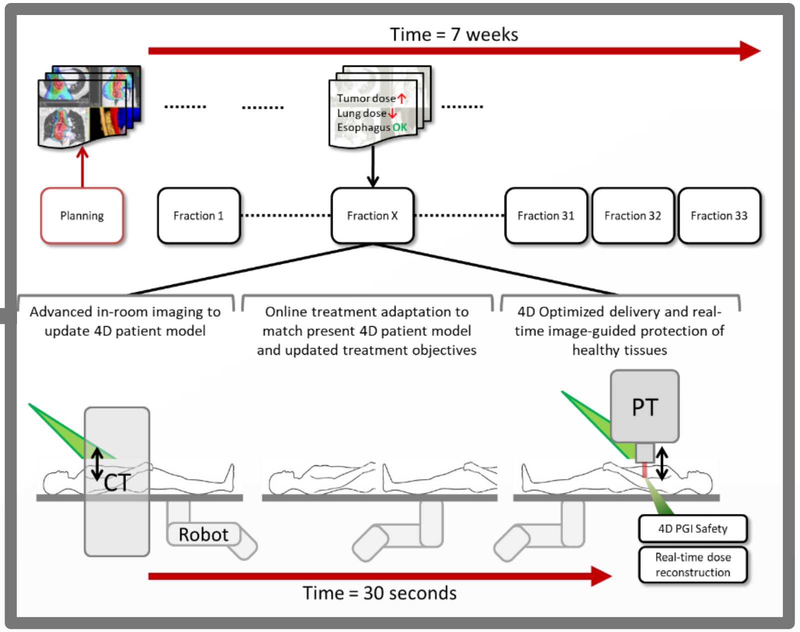
Kees Spruijt et al.

Growing tumor of 1 cm

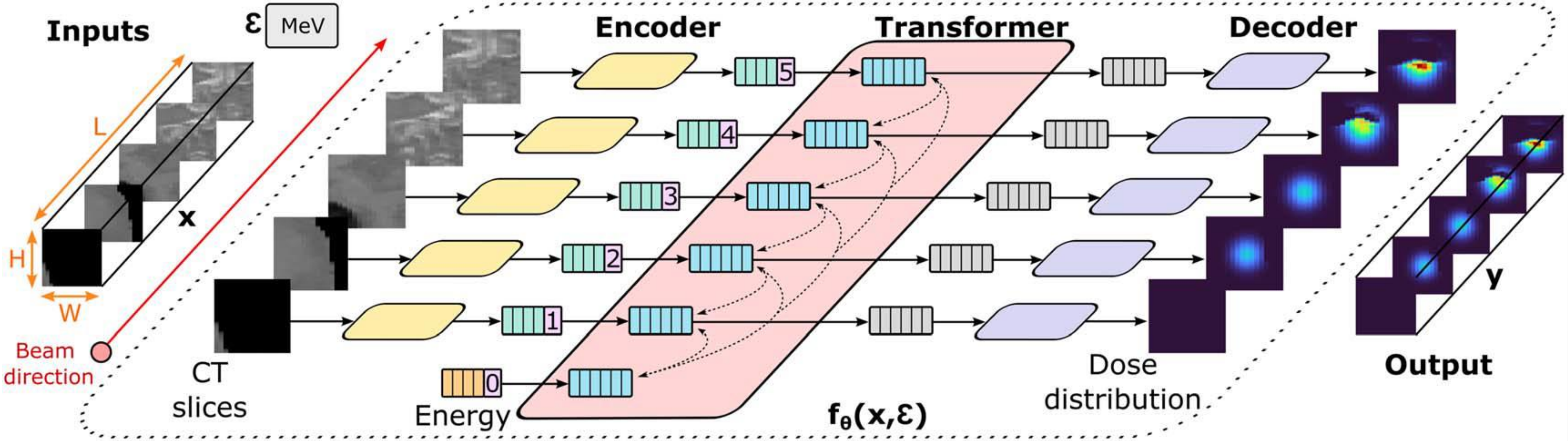


It Is an Engineering Challenge





Learning Particle Transport Physics



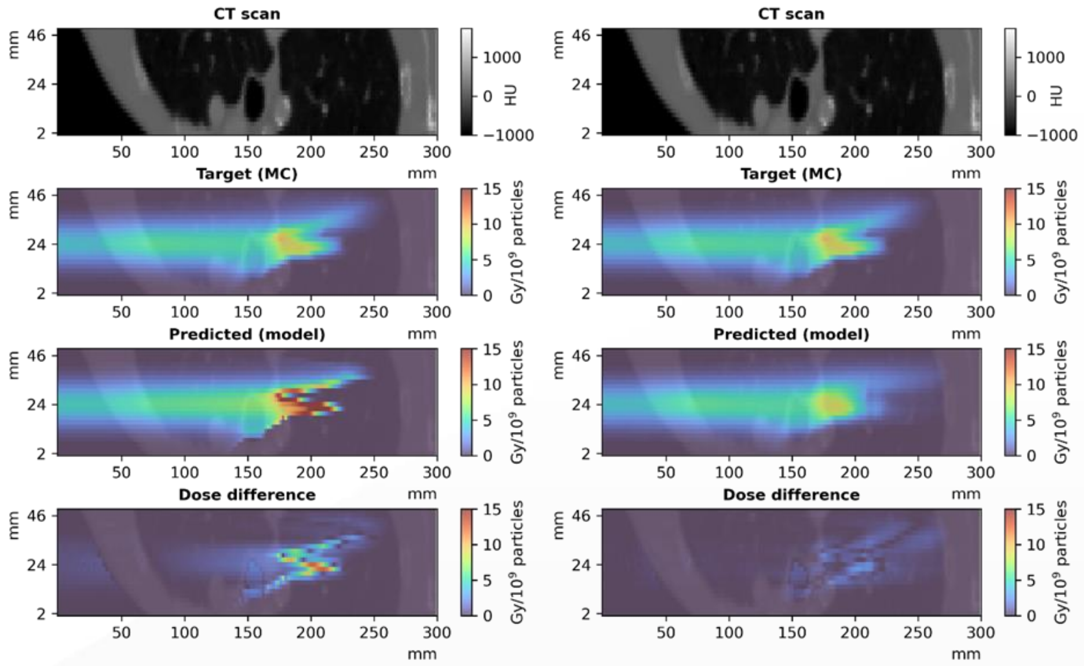
Pastor-Serrano O, Perkó Z. Millisecond speed deep learning based proton dose calculation with Monte Carlo accuracy. Phys Med Biol. 2022 May 9;67(10).

Millisecond Speed Proton Dose Calculation

On average 5 milliseconds

Close to Monte Carlo accuracy

Average gamma pass rate
Γ(3mm,1%) >99.4%



PB alternative

Proposed model

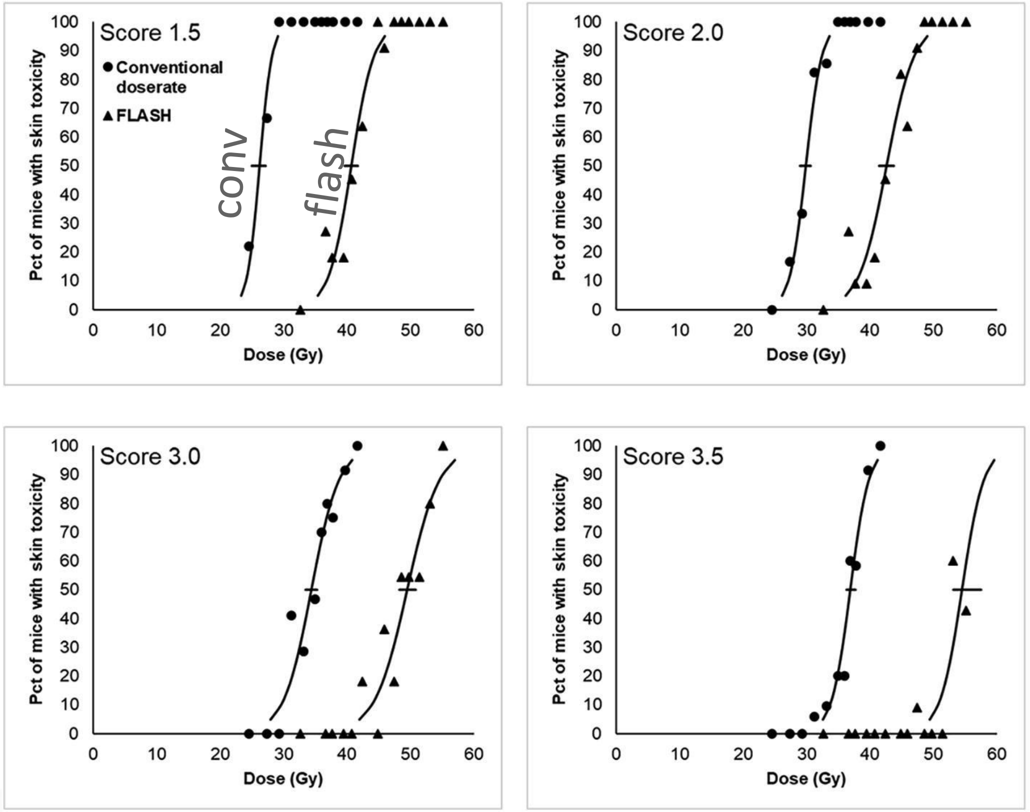
Pastor-Serrano O, Perkó Z. Millisecond speed deep learning based proton dose calculation with Monte Carlo accuracy. Phys Med Biol. 2022 May 9;67(10).

FLASH

A differential reduction of the radiosensitivity of healthy tissue relative to that of the tumor

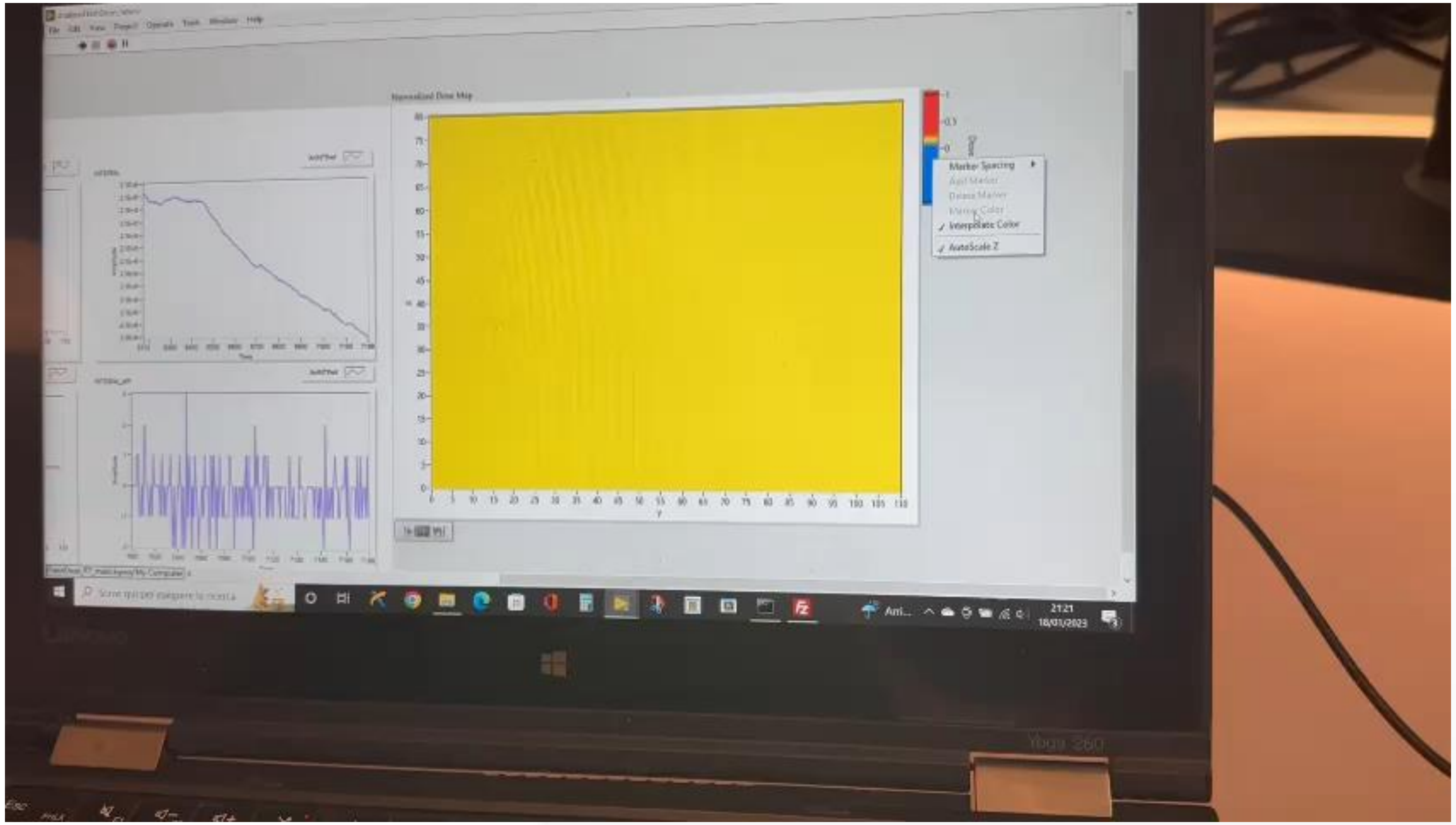
Ultra-high dose rate (> 40-100 Gy/s)

High dose (> 8 Gy) irradiation



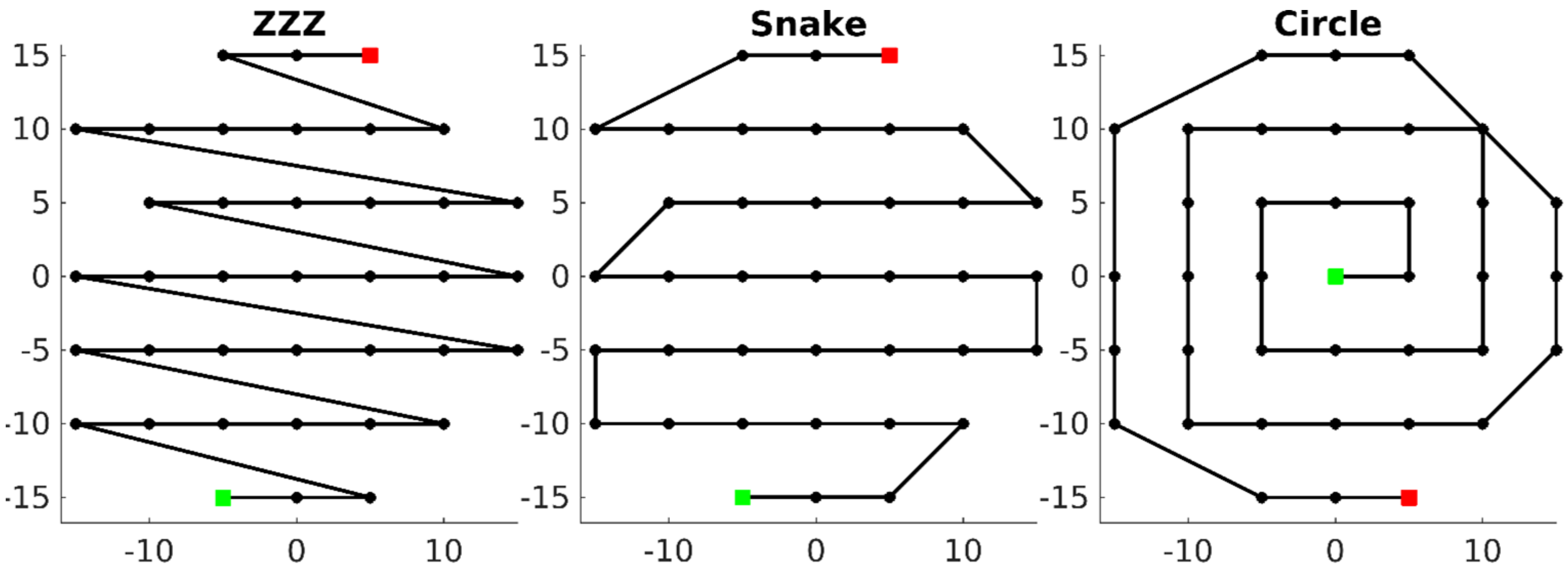
Singers Sørensen B, Krzysztof Sitarz M, Ankjærgaard C, Johansen J, Andersen CE, Kanouta E, Overgaard C, Grau C, Poulsen P. In vivo validation and tissue sparing factor for acute damage of pencil beam scanning proton FLASH. Radiother Oncol. 2021 Dec 22;167:109-115.

Scanning Beam



M. Rovituso et al.

Which Scan Pattern Is The FLASHiest?

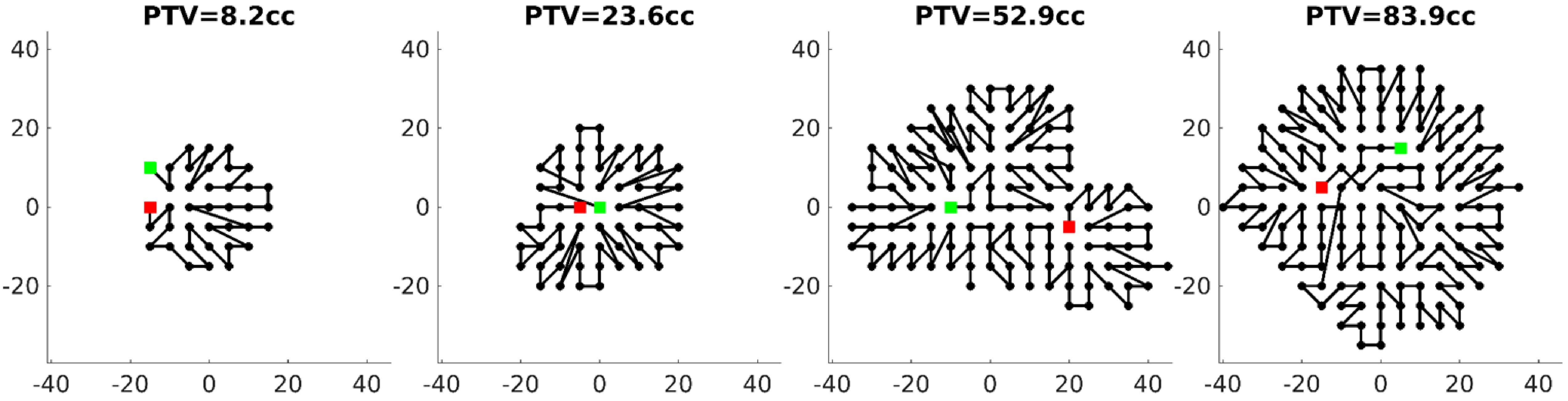


Rodrigo Jose Santo

TÉCNICO LISBOA

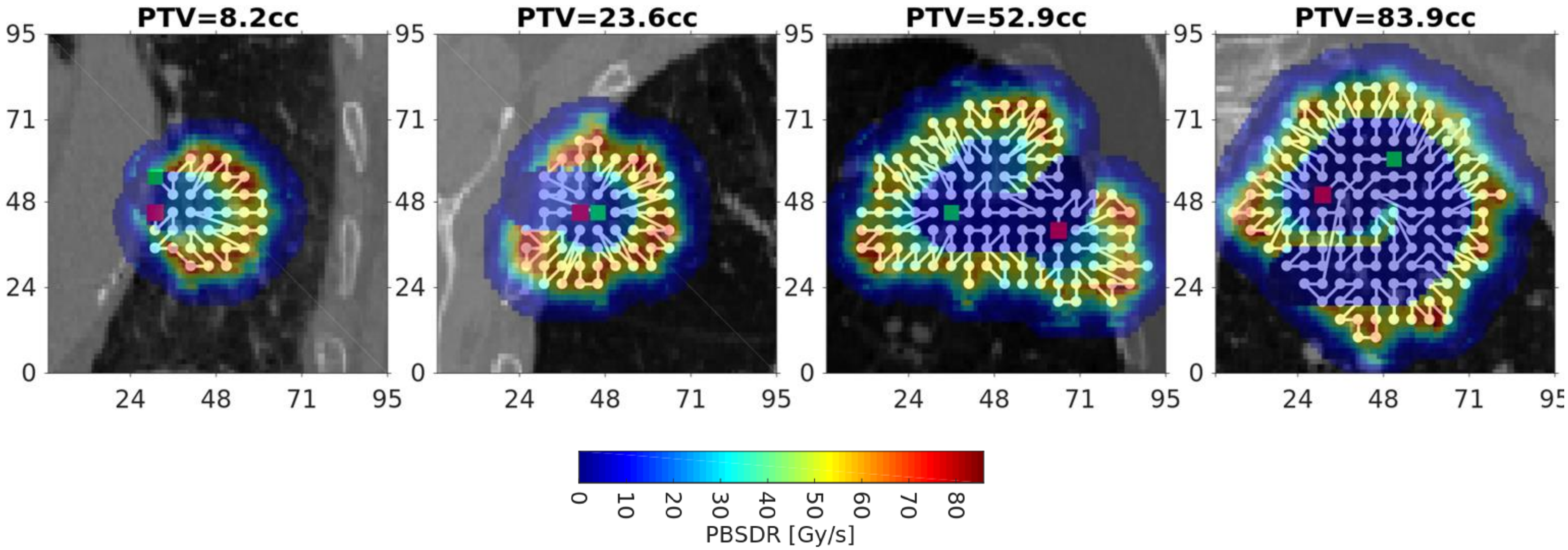
Erasmus MC

FLASH Optimized Patterns



37 spots → 159 spots

FLASH Optimized Patterns



TÉCNICO LISBOA

Erasmus MC

Conclusions

IMPT has been successfully implemented for moving (lung) tumors

Approach is probably still conservative and there is room for improvement

Interesting developments on ultra-high dose rate for motion mitigation and broadening of therapeutic window

Acknowledgements

Anne Lisa Wolf

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Danny Lathouwers

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Oscar Pastor Serrano

Steven Habraken

Erik Korevaar

Mirko Unipan

… and many others